INFORMATION DISCLOSURE STATEMENT (IDS)

Reference AG, i.e. JP 7-70182, of the IDS filed on March 29, 1999 was not considered by the Examiner for a lack of an English statement of its relevance or its English abstract. Applicants respectfully disagree. Applicants note that JP 7-70182 is equivalent to US 5,475,086, i.e. Reference AA, cited in the same IDS (according to your letter of March 27, 2000). Thus, the Examiner should be able to determine the relevance of JP 7-70182. Applicants respectfully request that the Examiner consider JP 7-70182 and send applicants a copy of the IDS with the Examiner's initials next to the citation of Reference AG.

Claim Objections

Claims 18-20 were rejected as improper multiple dependent claims. Applicants have amended claim 18 to make it not depend on any multiple dependent claim. Withdrawal of the objection is requested.

Claim Rejections – 35 U.S.C. 112, Second Paragraph

I. Claims 1-3 and 5 were rejected as indefinite because the Examiner urged that (1) "partial regions" and "amino acid sequences" recited in parts (h) and (i) should be recited in the singular. Applicants have accepted the Examiner's proposal and so amended the claims.

The Examiner also asserted that "essentially equivalent" in part (i) of claim 1 is vague. Applicants respectfully traverse the rejection. Applicants submit that one

skilled in the art would understand the meaning of "essentially equivalent" in part (i) of claim 1 because both the specificity and the affinity of the binding of a peptide to an MHC molecule can be determined without difficulties. The binding of peptides to MHC molecules is a reversible biomolecular interaction which has to be regarded as entirely analogous to the binding of a ligand to a receptor or the binding of an antigen to an antibody. For the review of the Examiner, applicants have attached copies of Berzofsky, *Fundamental Immunology*, Third Edition, Raven Press, pp. 421-443, 1993, and Malcherek, *Journal of Immunology*, vol. 153, pp. 1142-1149, 1994. Berzofsky and Malcherek support applicants' position and show that the binding of MHC molecules and peptide ligands can be analyzed by a relatively simple manner. Applicants have also attached a copy of Geluk, *Diabetes*, vol. 47, pp. 1594-1601, 1998, which confirms that those analyses are possible for a plurality of GAD peptides and MHC molecules without requiring undue efforts.

II. Claims 18-20 were rejected as indefinite for depending on the cancelled claim 4. Claim 18 has been amended to not depend on claim 4.

Withdrawal of the indefinite rejections is requested.

Claim Rejections – 35 U.S.C. 102

Claims 1-3, 5, 18 and 19 were rejected as lacking novelty due to Clare-Salzler (WO 95/07992) or Tobin (US 6,011,139). Applicants respectfully traverse the rejection.

Clare-Salzler or Tobin discloses two peptides of 20-amino-acid in length overlapping with some of the amino acids of SEQ ID NO:7 (see Sequence No. 37 and

38 in page 77, WO 95/07992; Sequence No. 37 and 38 in column 42, lines 32-33, US 6,011,139). However, Sequence No. 37 and 38 of Clare-Salzler or Tobin do not have isoleucine as the C-terminal amino acid. As a result, Clare-Salzler or Tobin does not anticipate the instant claims by failing to teach every limitation of part (h) of claim 1.

Withdrawal of the rejection is requested.

Claim Rejections – 35 U.S.C. 103

Claims 1-3, 5, and 18-20 were rejected as lacking inventive step over Clare-Salzler (WO 95/07992) or Tobin (US 6,011,139), in view of Burke (US 5,750,114). Applicants respectfully traverse the rejection.

The Office Action states that Clare-Slzler or Tobin does not teach putting cytokine as the accessory-stimulating component into the composition. The Examiner took a position that Burke teaches an HSV polypeptide vaccine further comprising cytokines and a pharmaceutically acceptable carrier (column 4, lines 7-38). Applicants note that Burke discloses a vaccine against Herpes Simplex Virus comprising recombinant HSV glycoproteins B and D (see the abstract). Because the recombinant HSV glycoproteins B and D are not related to the human glutamic acid decarboxylase (GAD), there would have been no motivation to modify the teachings of Clare-Salzler or Tobin by mixing any cytokine with the polypeptides of Clare-Salzler or Tobin for ameliorating GAD-associated autoimmune diseases. This is one of the reasons why the instant claims would not have been obvious over Clare-Salzler or Tobin in view of Burke.

Another reason why the instant claims would not have been obvious over Clare-Salzler or Tobin in view of Burke is that Clare-Salzler or Tobin does not teach the peptide of claim 1 since Sequence No. 37 and 38 of Clare-Salzler or Tobin do not have isoleucine as the C-terminal amino acid. Because Burke is silent on the amino acid sequences of Sequence No. 37 and 38, Burke provides no motivation to modify Sequence 37 and 38 of Clare-Salzler or Tobin by making isoleucine as the C-terminal amino acid. Thus, Clare-Salzler or Tobin in view of Burke fail to suggest or render obvious the invention of the instant claims.

Withdrawal of the obviousness rejection is requested.

Conclusion

With the above amendment and reasoning, applicants submit that the application is in a condition for allowance.

In the event this paper is not timely filed, applicants hereby petition for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300, along with any other additional fees which may be required with respect to this paper.

Respectfully submitted,
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Enclosures: Berzofsky, *Fundamental Immunology*, Third Edition, Raven Press, pp. 421-443, 1993;
Malcherek, *Journal of Immunology*, vol. 153, pp. 1142-1149, 1994; and
Geluk, *Diabetes*, vol. 47, pp. 1594-1601, 1998